

WHAT IS CLAIMED IS:

1. A therapeutic composition comprising a first agent that targets an interleukin-15 receptor (IL-15R) and a second agent that targets an interleukin-2 receptor (IL-2R).

2. The therapeutic composition of claim 1, wherein the first agent comprises a substantially pure mutant IL-15 polypeptide that binds a subunit of an IL-15R.

3. The therapeutic composition of claim 2, wherein the subunit is an IL-15R α subunit. 4. The therapeutic composition of claim 3, wherein the mutant IL-15 polypeptide has a mutation at position 156 of SEQ ID NO:2.

5. The therapeutic composition of claim 4, wherein the mutant IL-15 polypeptide also has a mutation at position 149 of SEQ ID NO:2.

6. The therapeutic composition of claim 4, wherein the mutation at position 156 of SEQ ID NO:2 is a substitution of aspartate for glutamine.

7. The therapeutic composition of claim 5, wherein the mutation at position 149 of SEQ ID NO:2 is a substitution of aspartate for glutamine.

8. The therapeutic composition of claim 5 wherein the mutant IL-15 polypeptide has a substitution of aspartate for glutamine at positions 149 and 156 of SEQ ID NO:2.

9. The therapeutic composition of claim 2, wherein the first agent further comprises a moiety that leads to the elimination of IL-15R-bearing cells.

10. The therapeutic composition of claim 9, wherein the moiety that lyses IL-15R-bearing cells is an Fc region of an IgG molecule.

11. The therapeutic composition of claim 1, wherein the first agent comprises a substantially pure anti-IL15R antibody.

12. The therapeutic composition of claim 1, wherein the second agent comprises an antibody that specifically binds IL-2 or an IL-2R.

5 13. A method of suppressing an immune response in a patient, the method comprising administering to the patient a therapeutic composition comprising a first agent that targets an IL-15R and a second agent that targets an IL-2R.

10 14. The method of claim 132, wherein the patient has an immune disease, particularly autoimmune disease or is at risk of developing an immune disease, particularly autoimmune disease.

15 15. The method of claim 14, wherein the autoimmune disease is a rheumatic disease selected from the group consisting of systemic lupus erythematosus, Sjögren's syndrome, scleroderma, mixed connective tissue disease, dermatomyositis, polymyositis, Reiter's syndrome, and Behcet's disease.

16. The method of claim 14, wherein the autoimmune disease is rheumatoid arthritis.

20 17. The method of claim 14, wherein the autoimmune disease is type I diabetes.

25 18. The method of claim 14, wherein the autoimmune disease is an autoimmune disease of the thyroid selected from the group consisting of Hashimoto's thyroiditis and Graves' Disease.

19. The method of claim 14, wherein the autoimmune disease is an autoimmune disease of the central nervous system selected from the group consisting of multiple sclerosis, myasthenia gravis, and encephalomyelitis.

20. The method of claim 14, wherein the autoimmune disease is a variety of pemphigus selected from the group consisting of pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, Senear-Usher syndrome, and Brazilian pemphigus.

5 21. The method of claim 14, wherein the autoimmune disease is psoriasis.

22. The method of claim 14, wherein the autoimmune disease is inflammatory bowel disease.

10 23. The method of claim 13, wherein the patient has acquired immune deficiency syndrome (AIDS).

24. The method of claim 13, wherein the patient has received a transplant of a biological organ, tissue, or cell.

15 25. The method of claim 13, wherein the patient has a graft versus host disease.

26. A method of eliminating a cell that expresses a receptor for IL-15, the method comprising exposing the cell to the therapeutic composition comprising a first agent that
20 targets an IL-15R and a second agent that targets an IL-2R.

27. The method of claim 26, wherein the cell is a cell of the immune system.

28. The cell of claim 26, wherein the cell is a malignant cell.

25 29. A method of diagnosing a patient as having a disease or condition that can be treated with the therapeutic composition of claim 1, the method comprising determining whether a biological sample obtained from the patient contains a cell that is bound by a polypeptide comprising IL-15 and an antigenic tag, the occurrence of binding indicating that
30 the cell can be bound by an agent that targets an IL-15R *in vivo* and thereby inhibited from proliferating in response to wild-type IL-15 *in vivo*.

30. A pharmaceutically acceptable composition comprising two or more agents, each of which promote T cell death.

5 31. The pharmaceutical composition of claim 30, further comprising an agent that inhibits T cell proliferation.

10 32. The pharmaceutical composition of claim 31, wherein the composition comprises a lytic IL-2/Fc molecule, a mutant IL-15 molecule that antagonizes and IL-15 receptor, and rapamycin.

33. A pharmaceutically acceptable composition comprising at least one agent that promotes T cell death and at least one agent that inhibits T cell proliferation.

15 34. The pharmaceutical composition of claim 32, wherein the T cell death is AICD (activation induced cell death), passive cell death, ADCC (antibody dependent cell-mediated cytotoxicity) or CDC (complement directed cytotoxicity).